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09 1039,177

MAR 13, 1998

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United States Patent Number **6692,925**, column \_\_\_\_\_, line, \_\_\_\_\_ or \_\_\_\_\_.

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(12) **United States Patent**  
Miyazono et al.

(10) **Patent No.:** US 6,692,925 B1  
(45) **Date of Patent:** Feb. 17, 2004

- (54) **PROTEINS HAVING SERINE/THREONINE KINASE DOMAINS, CORRESPONDING NUCLEIC ACID MOLECULES, AND THEIR USE**
- (75) **Inventors:** Kohei Miyazono, Shiki (JP); Takeshe Imamura, Tokyo (JP); Peter ten Dijke, Amsterdam (NL)
- (73) **Assignee:** Ludwig Institute for Cancer Research, New York, NY (US)
- (\*) **Notice:** Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

- (21) **Appl. No.:** 09/267,963  
(22) **Filed:** Mar. 12, 1999

**Related U.S. Application Data**

- (63) Continuation-in-part of application No. 09/039,177, filed on Mar. 13, 1998, now abandoned, which is a continuation-in-part of application No. 08/436,265.
- (60) Provisional application No. PCT/GB93/02367, filed on Nov. 17, 1993, now Pat. No. 6,316,217.

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- (51) **Int. Cl.<sup>7</sup>** ..... G01N 33/53; C07K 14/495; C07K 16/22; C07K 16/28; C12P 21/02
- (52) **U.S. Cl.** ..... 435/7.2; 435/7.21; 435/69.1; 435/69.7; 435/325; 530/350; 530/388.22; 530/388.23; 530/387.1; 530/389.2
- (58) **Field of Search** ..... 435/7.1, 7.2, 7.21, 435/7.6, 69.1, 69.7, 325; 530/350, 387.1, 388.22, 388.23, 389.2

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(57) **ABSTRACT**

The invention relates to the molecule referred to as ALK-1, and its role as a type I receptor for members of the TGF- $\beta$  family. The molecule has a role in the phosphorylation of Smad-5 and Smad1, which also act as activators of certain genes. Aspects of the invention relate to this interaction.